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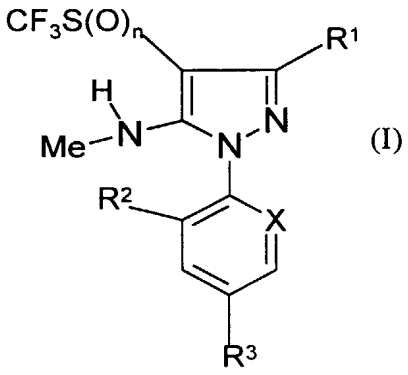
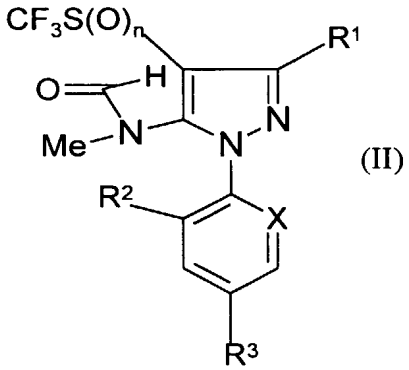
(54) Title: PROCESS FOR THE PREPARATION OF PESTICIDAL COMPOUNDS



(I)



(II)

(57) Abstract: A process for the preparation of a compound of general formula (I), wherein R^1 is CN or $CSNH_2$; R^2 is hydrogen or chloride; and R^3 is halogen or haloalkyl or haloalkoxy or SF_5 which process comprises reacting a compound of formula (II), where R^1, R^2 and R^3 are as defined above; with a proton source.

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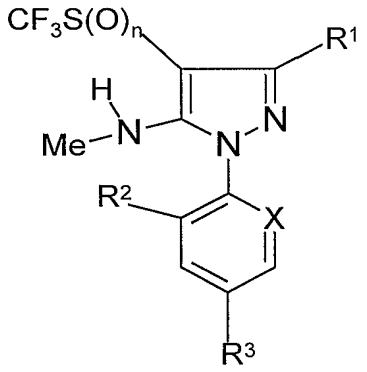
PROCESS FOR THE PREPARATION OF PESTICIDAL COMPOUNDS

The present invention relates to a process for the preparation of substituted pyrazole compounds.

Pyrazoles such as 5-Amino-1-aryl-3-cyanopyrazole compounds and derivatives thereof, for example Fipronil, form an important class of insecticides. Certain substituted 5-N-alkyl-N-alkoxyacetylamino-1-aryl-3-cyanopyrazole compounds have valuable pesticidal properties as disclosed in WO 00/35884 and US Patent 5,556,873.

We have developed a new synthesis route for the production of intermediate compounds useful in the preparation of substituted pyrazole pesticide compounds.

Accordingly, the present invention provides a process for the preparation of a compound of general formula (I)



(I)

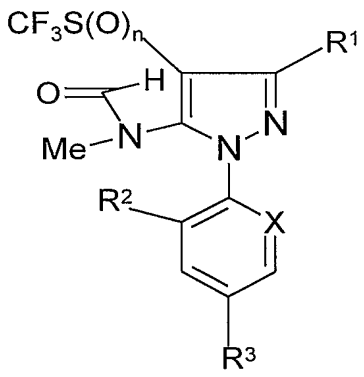
wherein

R^1 is CN or $CSNH_2$;

R^2 is hydrogen or chloride; and

R^3 is halogen or haloalkyl or haloalkoxy or SF_5

which process comprises reacting a compound of formula (II)



(II)

where R^1, R^2 and R^3 are as defined above; with a proton source.

The proton source used in the process of the present invention is preferably an aqueous acidic solution for example aqueous hydrogen chloride.

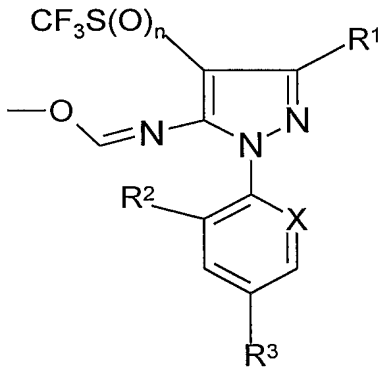
The reaction is suitably carried out in a suitable solvent or in a solvent which may or may not be partially miscible with water. Suitable solvents include hydrocarbon solvents such as toluene or xylene.

The amount of proton source used in the reaction is suitably from 0.1 to 2 equivalents, preferably from 0.5 to 1.0 equivalents.

The reaction may suitable be carried out at a temperature of from minus 50 to 200 °C, preferably from 50 to 100°C.

With regard to R^1, R^2 and R^3 , R^1 is preferably CN, R^2 is preferably chloride and R^3 is preferably a haloalkyl, especially trifluoromethyl.

Compound (II) may be prepared by a novel synthesis route and according to another aspect of the present invention there is provided a process for the preparation of compound (II) as defined above which process comprises reacting a compound of general formula (III)



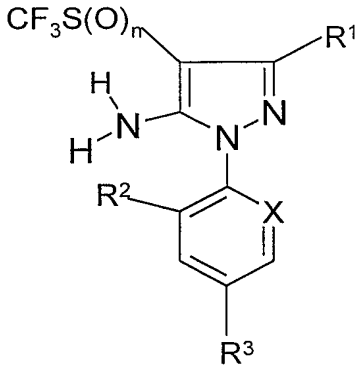
(III)

wherein R1, R2 and R3 are as previously defined; with a quaternary ammonium salt

The quaternary ammonium salt may be a tetraalkylammonium halide such as the iodide or the bromide, preferably tetraalkylammonium bromide. Suitable tetraalkylammonium bromide include tetrabutylammonium Bromide. The amount of the halide salt used in the reaction is suitably from 0.01 to 2 equivalents, preferably from 0.1 to 0.5 equivalents.

The reaction may be carried out in the presence of an organic solvent which may or may not be partially miscible with water. Suitable solvents include hydrocarbon solvents such as toluene or xylene. The reaction is suitably carried out at a temperature of from 50 to 100°C.

Compound (III), as defined above, may be prepared by the known synthesis route which comprises reacting a pyrazole compound known as fipronil having the formula (IV)

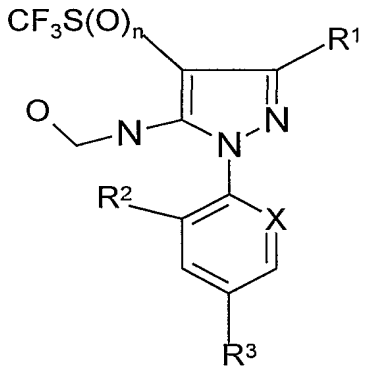


(IV)

with trimethylorthoformate. This reaction may be carried out the presence of an acidic catalyst. Suitable catalyst include para-toluene sulphonic acid.

Compound (III) may also be treated with the quaternary ammonium salt followed by acidic treatment to produce directly compound (I) without isolating compound (II).

Compound (I) may also be prepared by reacting fipronil (compound IV) with formaldehyde or a formaldehyde trimer or the chemical equivalent thereof to produce an intermediate compound (V)



(V)

where R1, R2, R3 are as defined above.

Intermediate compound (V) may then be reacted with a reducing agent to provide compound (I). A suitable reducing agent includes sodium borohydride. The reducing agent may be present in an amount of from 1 to 5 equivalents.

Certain compounds according to formulae (II), (III) and (V) are novel compounds and in particular according to another aspect of the present invention there is provided novel compounds:

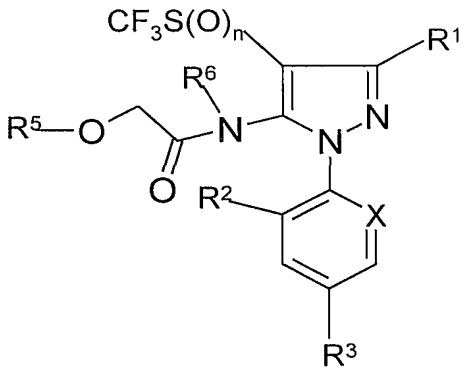
3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-N-formyl-N-methylamino-4-trifluoromethylsulfinylpyrazole (Compound II).

3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-methoxy methylideneamino-4-trifluoromethylsulfinylpyrazole (Compound III)

3-cyano-1,(2,6-dichloro-4-trifluoromethylphenyl)-5-hydroxymethylamino-4-trifluoromethylsulphinylpyrazole (Compound V).

Compound (I) prepared according to the process of the present invention may be used as the starting material for a further important pyrazole which is

known to have pesticidal properties and which is defined according to general formula (VI).



(VI)

wherein

R^1 is CN or $CSNH_2$;

X is N or CR^4;

R^2 and R^4 are, each, independently hydrogen or chlorine;

R^3 is halogen, haloalkyl, haloalkoxy or $-SF_5$;

R^5 and R^6 are each independently an alkyl group; and

n is 0, 1 or 2;

The preparation of this compound from compound (I) is known from International Patent Application Number WO 00/35884 which is herein incorporated by reference. In particular compound (I) is reacted with ethoxy acetyl chloride in the presence of triethylamine to produce compound (VI).

The present invention will now be illustrated by reference to the following non limiting examples:

Example 1:

A substantial molar excess of trimethylorthoformat is reacted with fipronil (Compound IV) at reflux with 0.5 equivalents of paratoluensulfonic acid to provide 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-methoxymethylideneamino-4-trifluoromethylsulfinylpyrazole (Compound III).

This product is immediately treadted with 0.1 equivalents of tetrabutylammonium iodide in xylenes at 100 degrees centigrade for 5 hours to provide 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-(N-formyl-N-

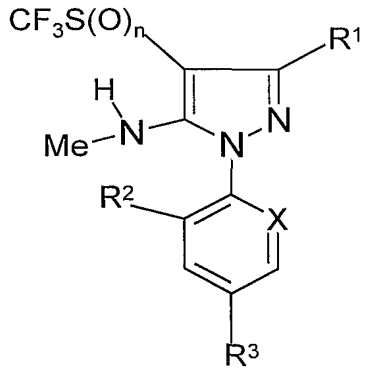
methylamino)-4-trifluoromethylsulfinylpyrazole (Compound II). The medium is immediately reacted with aqueous hydrogen chloride and to provide 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-methylamino-4-trifluoromethylsulfinylpyrazole as final product (Compound I).

Example 2:

5 equivalent of a sodium methylate (30% solution in methanol) was rapidly added to a suspension of 0.437g of Fipronil and 1.4 equivalent of paraformaldehyde in 3mL of methanol to provide the 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-hydroxymethylamino-4-trifluoromethylsulfinylpyrazole (Compound V) after 3 hour at 20°C and 1 hour at 60°C. Then 1 equivalent of sodium borohydride was added to the medium which provide after classical extraction and chromatography separation the 3-Cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-methylamino-4-trifluoromethylsulfinylpyrazole (Compound I).

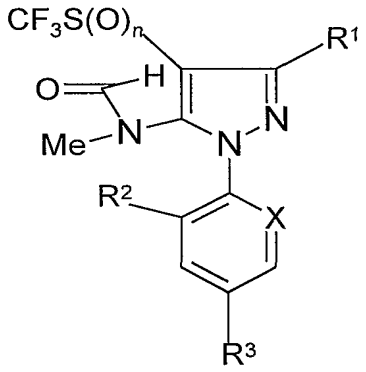
Claims

1. A process for the preparation of a compound of general formula (I)



(I)

wherein R^1 is CN or $CSNH_2$; R^2 is hydrogen or chloride; and R^3 is halogen or haloalkyl or haloalkoxy or SF_5 which process comprises reacting a compound of formula (II)



(II)

where R^1, R^2 and R^3 are as defined above; with a proton source.

2. A process as claimed in claim 1 in which R^1 is CN, R^2 is chloride and R^3 is trifluoromethyl.

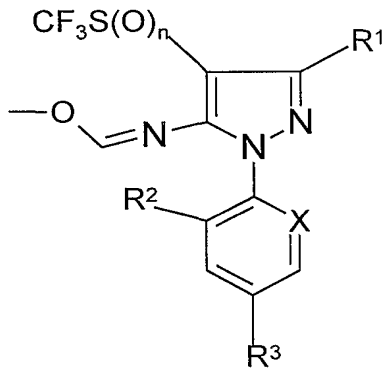
3. A process as claimed in claim 1 or claim 2 in which the proton source is an aqueous acidic solution.

4. A process a s claimed in claim 3 in which the aqueous acidic solution is aqueous hydrogen chloride.

5. A process as claimed in any one of the preceding claims carried out in the presence of a solvent.

6. A process a s claimed in claim 5 in which the solvent is toluene or xylene.

7. A process for the preparation of compound (II) as claimed in claim 1 which process comprises reacting a compound of general formula (III)



(III)

wherein R^1, R^2 and R^3 are as defined in claim 1; with a quaternary ammonium salt

8. A process as claimed in claim 7 in which the quaternary ammonium salt is a tetraalkylammonium halide

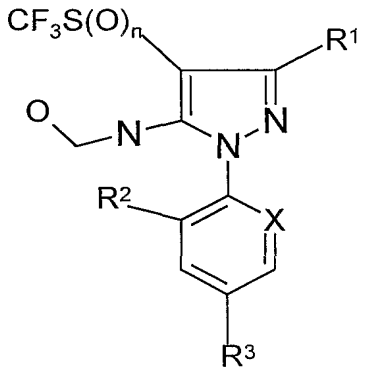
9. A process as claimed in claim 7 or 8 in which the tetraalkylammonium halide is tetraalkylammonium bromide.

10. A process as claimed in any one of claims 7 to 9 carried out in the presence of an organic solvent.

11. A process as claimed in claim 10 in which the solvent is toluene or xylene.

12. A process for the preparation of compound (I) as defined in claim 1 which comprises reacting compound (III) as defined in claim 6 with a quaternary ammonium salt followed by the addition of an acid.

13. A process for the preparation of compound (I) as defined in claim 1 which comprises a first step of reacting fipronil with formaldehyde or a formaldehyde trimer or the chemical equivalent thereof to produce an intermediate compound (V)



(V)

wherein R^1, R^2 and R^3 are as defined in claim 1; and a second step of reacting compound (V) with a reducing agent.

14. A process as claimed in claim 13 in which the reducing agent is sodium borohydride.

15. Novel compound 3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-N-formyl-N-methylamino-4-trifluoromethylsulfinylpyrazole.

16. Novel compound 3-cyano-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-methoxy methylideneamino-4-trifluoromethylsulfinylpyrazole.

17. Novel compound 3-cyano-1,(2,6-dichloro-4-trifluoromethylphenyl)-5-hydroxymethylamino-4-trifluoromethylsulphinylpyrazole.